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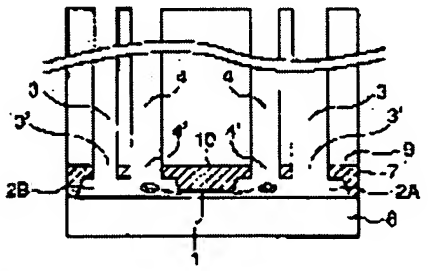
## (54) APPARATUS FOR DETECTING CHEMOTAXIS OF CELL AND FOR ISOLATING CHAMOTACTIC CELL

(57)Abstract:

PROBLEM TO BE SOLVED: To provide an apparatus that permits accurately and easily detecting the chemotaxis of a cell by a chemotactic factor or the inhibition of chemotaxis of a cell by an inhibitor to chemotaxis by accurately and easily detecting the movement of a cell for itself using a small amount of specimen and for isolating such a cell.

SOLUTION: This apparatus for detecting the chemotaxis of a cell and for isolating a chemotactic cell is an apparatus having wells connected one another via paths, wherein each path has a tube for injecting or collecting a specimen and a tube for avoiding the elevation or reduction of the pressure caused by the injection or collection of the specimen.




1: 試料
2: ウェル
3: 試料注入・採取用管
3': 管3に対応する貫通孔
4: 試料の注入・採取時における昇圧・減圧を回避するための管
4': 管4に対応する貫通孔
6: 基板
7: ポリカ基板
9: 管を挿入するための
10: 上部



LEGAL STATUS

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CLAIMS

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[Claim(s)]
[Claim 1] two or more wells are mutually open for free passage through passage -- and -- each -- the cell chemotaxis detection characterized by having tubing for avoiding the pressure up or reduced pressure by tubing for a well pouring in or extracting a sample, impregnation of a sample, or extraction, and **-ized cellular segregation equipment.
[Claim 2] Cell chemotaxis detection according to claim 1 and **-ized cellular segregation equipment which are characterized by two or more wells being open for free passage to the serial through passage.
[Claim 3] Cell chemotaxis detection according to claim 1 and **-ized cellular segregation equipment which are characterized by two or more wells being open for free passage through passage to one well.
[Claim 4] Cell chemotaxis detection according to claim 3 and **-ized cellular segregation equipment which are characterized by at least two wells being further open for free passage with other common wells through passage among two or more wells which are open for free passage through passage to one well.
[Claim 5] Cell chemotaxis detection according to claim 1 to 4 and **-ized cellular segregation equipment which are characterized by intersecting perpendicularly with passage and establishing a wall in either or the both sides of a well which is mutually open for free passage through passage in order to restrict the amount of a liquid [ / near the passage ].

[Claim 6] Cell chemotaxis detection according to claim 1 and **-ized cellular segregation equipment which passage is the bank which forms a slit and are characterized by having a terrace if needed.
[Claim 7] Cell chemotaxis detection of claim 6 publication and **-ized cellular segregation equipment which are characterized by establishing the slot of the width of face doubled with the bank at the path of a cell, or its deformability in 1 thru/or the obstruction constituted two or more in passage.
[Claim 8] Cell chemotaxis detection according to claim 7 and **-ized cellular segregation equipment which are characterized by two or more slots of the direction which goes to the well which faces in passage being mutually open for free passage in 1 thru/or two or more slots which intersects perpendicularly with this.
[Claim 9] Cell chemotaxis detection according to claim 8 and **-ized cellular segregation equipment which are characterized by changing gradually [ whenever the width of face of two or more slots of the direction which goes to the well which faces in passage crosses 1 thru/or two or more slots which intersects perpendicularly with this ].
[Claim 10] Cell chemotaxis detection according to claim 8 or 9 and **-ized cellular segregation equipment which are characterized by shifting a mutual location whenever two or more slots of the direction which goes to the well which faces in passage cross 1 thru/or two or more slots which intersects perpendicularly with this, and forming them.
[Claim 11] Cell chemotaxis detection according to claim 7 to 10 and **-ized cellular segregation equipment which are characterized by forming in two places the train of the obstruction which prepares a terrace in the center of a bank and constitutes a slot across a terrace in passage.
[Claim 12] Cell chemotaxis detection according to claim 6 to 11 and **-ized cellular segregation equipment which are characterized by forming in multistage the terrace of the bank established in passage.
[Claim 13] Cell chemotaxis detection according to claim 6 and **-ized cellular segregation equipment which are characterized by establishing the slot of the width of face doubled with the bank at the path of a cell, or its deformability in 1 thru/or the obstruction constituted two or more in passage, and forming the terrace in a bank multistage.
[Claim 14] Cell chemotaxis detection and **-ized cellular segregation equipment which make one unit each of cell chemotaxis detection according to claim 1 to 13 and **-ized cellular segregation equipment, and are characterized for the same or the accumulation unit which comes to accumulate two or more two or more sorts of units by 1 or having more than one.
[Claim 15] One of the unit unit which consists of cell chemotaxis detection according to claim 1 to 13 and **-ized

cellular segregation equipment The same or the unit section which consists of the accumulation unit or two or more accumulation units which it makes it come to pile up two or more two or more sorts of units, The cell supply pipet which moves each part, such as a cell stores dept., a specimen stores dept., and this, [ whether it unites with the unit section and the detecting element which detects migration of the cell in a specimen supply pipet and the unit section, and records a detection result if needed is prepared, and ] or the device which prepares so that it can respond to two or more unit sections, and controls migration of a cell supply pipet and a specimen supply pipet -- and Cell chemotaxis detection and **-ized cellular segregation equipment which are characterized by having the device for moving the following unit section to the location of the line of flow of a pipet if needed while moving the unit section to a detecting element and which were automated.

[Claim 16] Cell chemotaxis detection according to claim 15 and **-ized cellular segregation equipment which are characterized by being controlled to have the pipet washing section, and for a pipet to set in the pipet washing section, and to attract and discharge a penetrant remover and which were automated.

[Claim 17] It is controlled so that a cell supply pipet attracts after stirring the cell suspension of the amount beforehand defined from the cell stores dept. if needed and supplies this to the unit section, It is controlled for a specimen supply pipet to attract the specimen of the amount beforehand defined from the specimen stores dept., and to supply this to the unit section, to carry out pumping of the penetrant remover and to wash it in the pipet washing section, subsequently, the well of a cell to which it responded at the time of the need, and the specimen supply pipet was previously supplied before specimen supply actuation -- the automated cell chemotaxis detection according to claim 16 which is characterized by being controlled to attract the liquid of the specified quantity in order to adjust an inner location, and **-ized cellular segregation equipment.

[Claim 18] a chemotactic factor content solution [ as opposed to / in cell chemotaxis detection according to claim 1 to 17 and **-ized cellular segregation equipment, put the mixed suspension of two or more sorts of cells into one well, and / the cell of specification / other wells ] -- putting in -- being concerned -- others -- the separation approach of the **-ized cell characterized by extracting the cell which moved to the well.

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## DETAILED DESCRIPTION

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[Detailed Description of the Invention]
[0001]
[Field of the Invention] This invention is concerned with the equipment for carrying out counting of the judgment of whether to move in the direction where a cell is fixed by itself, the observation in the condition of moving in the direction where a cell is fixed by itself, or the number of the cells which moved in the fixed direction by themselves, i.e., cell chemotaxis detection equipment. Furthermore, this invention is concerned with the decollator of the cell using a cell moving in the fixed direction by itself alternatively, and the separation approach of the cell using it.
[0002]
[Description of the Prior Art] It is in vitro about the chemotaxis of a cell. The Boyden chamber has been used as equipment to detect. This is equipment which observes the number which it has the structure made into the top room and the bottom room for 2 minutes with the filter with which the hole (diameter of 3-8 micrometers) of the magnitude which can pass a cell has opened, the specimen solution which contains cell suspension at a top room and contains a chemotactic factor at a bottom room was put in, and the cell which moves toward a chemotactic factor passed the filter, or appeared in the rear face. Although it is equipment currently used today most ordinarily, 1/4ml-1 / 20ml of suspension of 1x106 cells/ml concentration are required as an amount of cell suspension. This means making it the number of cells and needing at least 5x104 pieces. When aimed at the cell obtained so much, particular problem cannot be found, but about 1 to 5%, basophilic leucocyte is the same, 1% or less and monocyte are the same, and it is about 1 - 2%, and when aimed at such a cell that recognizes little chisel existence, the rate of occupying eosinophile leucocyte to a deletion blood leucocyte requires many efforts, for example, in order to get an initial complement. Moreover, when using a mite like a mouse, the amount which can collect blood is restricted, hits one animal, and is about at most 0.7ml. Furthermore, there is a cell which is hard to come to hand so much also in the cell which exists in a cancer cell or an organization, and investigating the property is expected for there to be little amount used. Moreover, in a Boyden chamber, the observation of the condition of a cell or the number in the process which moves of counting cannot be carried out.
[0003] The slide glass for quality which can observe **-ization of a cell on some level is marketed. As for this, two slots with width of face of 4mm, a die length [ of 25mm ], and a depth of 1mm are prepared across the bank (passage) of 1mm width of face on the slide glass. Cell suspension is put into one slot, the specimen solution containing a chemotactic factor is put into the slot on another side, and the cell which moves to the slot on another side across a bank from one slot is observed under a microscope. In case cell suspension and a specimen solution are put into each slot, this product takes delicate accommodation, in order for liquid to overflow from each slot and to make it not flow into the slot on another side. Moreover, the volume of one slot is 100microl and 1/10ml cell suspension is required at least.
[0004] On a slide glass, two wells are prepared in concentric circular, and the chemotaxis chamber which separated the meantime on the bank (passage) is marketed (weber scientific company). Cell suspension is put into an inside well, it puts a specimen into an outside well, respectively, and this puts a cover glass, and observes under a microscope the cell which passes mounting. 20 micrometers of banks are low set up from the cover glass, and a cell passes through the clearance. the case where this equipment is used -- each -- the time of it being necessary to carry out delicate accommodation and so that liquid may not overflow, and an oil level rising, and putting a cover glass, when putting cell suspension or a specimen into a well -- both -- it tends to happen that the liquid of a well overcomes a bank and is mixed. Therefore, it is difficult to remain in observing **-izing and migration of a cell, and to perform the existence and the quantum of **-izing and migration with this equipment.
[0005] Equipment equipped with the passage which comes to prepare two or more detailed slots in a silicon single

crystal substrate front face using a semi-conductor production technique for measurement of a hemorheology is proposed (Kikuchi living thing physics besides others, SPIE Vol.2978, 165-171 (1997), and Kikuchi 214 No. 254-258 (1997)). Although this makes it possible to make the flow of blood cell suspension, to observe and study the situation of a blood flow, and to observe the behavior in cell level by giving differential pressure across passage, it has not aimed at observing thru/or measuring migration by own strength of a corpuscle.

[0006] In the direction which intersects perpendicularly with JP,3-257366,A to the straight line which connects said input and tap hole to the obstruction which arranges to juxtaposition the big slot which has input in the end section and has a tap hole in the other end, and divides this slot, the blood circuits in which it comes to prepare the minute slot which opens both slots for free passage are indicated. This passes the specimen which contains a blood sample in one of the big slots, and contains a chemotactic factor in the slot of a sink and another side, leads a part of blood sample to a detailed slot (passage), is detecting the cell which passes through a detailed slot (passage), and checks a motion and function of a cell, or observes and measures migration nature. In order to make the flow through which the specimen which contains a blood sample and a chemotactic factor by the big slot circulates, a blood sample and a specimen are considerable-amount need, and it is unsuitable for investigating the property of a cell using a minute amount sample.

[0007]

[Problem(s) to be Solved by the Invention] In detecting the chemotaxis of the cell by the chemotactic factor, or chemotaxis inhibition of the cell by the chemotactic factor inhibitor, this invention aims at offering the equipment which can detect the motion based on own strength of a cell correctly and easily. It is an important matter, in order for the motion based on own strength to mean the condition that a cell moves by its movement, without being influenced of a pressure etc. here and to detect an operation of a chemotactic factor with high reliability. for that purpose, samples, such as cell suspension and a specimen solution, -- each -- not to be mixed mutually is required in case it is poured into a well. Moreover, this invention aims at offering the equipment which can detect the chemotaxis of a cell using a small amount of cell sample. In addition, this invention aims at offer of the equipment with which the matter which checks the chemotaxis matter of a cell and it is searched. Furthermore, this invention offers one of the purposes the equipment which can catch a motion of a cell on each level. This invention also sets to one of the purpose of the at once to offer the equipment which can perform detection and measurement automatically about many specimens. This invention also sets to one of the purpose of the to offer the equipment which carries out separation extraction of the specific cell alternatively from the mixed liquor of two or more sorts of cells.

[0008]

[Means for Solving the Problem] two or more wells are opening the equipment of each other in connection with this invention for free passage through passage -- and -- each -- it is the cell chemotaxis detection and **-ized cellular segregation equipment which are characterized by having tubing for avoiding the pressure up or reduced pressure by tubing for a well pouring in or extracting a sample, impregnation of a sample, or extraction.

[0009] Two or more wells may be open for free passage to the serial through passage, and two or more wells may be open for free passage through passage to one well. Furthermore, at least two of two or more wells which are open for free passage through passage at one well in the case of the latter may be mutually open for free passage with other common wells further through passage.

[0010] In at least one of the wells, such as this, in order to restrict the amount of a liquid [ / near the passage ], it can intersect perpendicularly with passage and a wall can be established.

[0011] In this invention, desirable passage is a bank which forms a slit and it is desirable to establish the slot of the width of face doubled with the path of a cell or its deformability in a bank for two or more [ 1 thru/or ], for example, the obstruction constituted about 100. You may change gradually [ whenever the width of face of two or more slots of the direction which goes to the well which two or more slots of the direction which goes to the well which faces in passage may be mutually open for free passage in 1 thru/or two or more slots which intersects perpendicularly with this, and face crosses the slot which intersects perpendicularly with this ]. . Furthermore, physical relationship mutual whenever it crosses the slot which intersects perpendicularly with this is shifted, for example, two part carries out [ 1 pitch ** ], and two or more slots of the direction which goes to the well which faces may be formed.

[0012] Moreover, the terrace may be established in the bank and the terrace may be formed in multistage. A terrace is prepared in the center of a bank and the train of the obstruction which constitutes a slot across a terrace may be formed in two places.

[0013] the accumulation unit on which cell chemotaxis detection of this invention and **-ized cellular segregation equipment made each above equipment one unit, and two or more same or two or more sorts of units were made to accumulate -- 1 -- or it can have more than one. This is useful in order to process many specimens to coincidence, and to detect the chemotaxis of the cell of a large number or a variety to coincidence or to separate various cells at once.

[0014] One of the unit unit which this invention becomes from the above-mentioned cell chemotaxis detection and **-ized cellular segregation equipment The same or the unit section which consists of the accumulation unit or two or more accumulation units which it makes it come to pile up two or more two or more sorts of units, The cell supply pipet which moves each part, such as a cell stores dept., a specimen stores dept., and this, [ whether it unites with the unit section and the detecting element which detects migration of the cell in a specimen supply pipet and the unit section, and records a detection result if needed is prepared, and ] or the device which prepares so that it can respond to two or more unit sections, and controls migration of a cell supply pipet and a specimen supply pipet -- and If needed, while moving the unit section to a detecting element, the cell chemotaxis detection and **-ized cellular segregation equipment equipped with the device for moving the following unit section to the location of the line of flow of a pipet which were automated are included. Here, not only glass but a metal, plastics, etc. can be used for the quality of the material of a pipet, choosing them suitably.

[0015] Furthermore, this invention can include the device controlled to have the pipet washing section, and for a pipet to set in the pipet washing section, and to attract and discharge a penetrant remover if needed.

[0016] It is controlled for this invention to attract after stirring the cell suspension of the amount as which the cell supply pipet was beforehand determined from the cell stores dept. if needed, and to supply this to the unit section, It is controlled for a specimen supply pipet to attract the specimen of the amount beforehand defined from the specimen stores dept., and to supply this to the unit section, to carry out pumping of the penetrant remover and to wash it in the pipet washing section, subsequently, the well of a cell to which it responded at the time of the need, and the specimen supply pipet was previously supplied before specimen supply actuation -- in order to adjust an inner location, it is the cell chemotaxis detection and **-ized cellular segregation equipment including being controlled to attract the liquid of the specified quantity which were automated.

[0017] a chemotactic factor content solution [ as opposed to / this invention puts the mixed suspension of two or more sorts of cells into one well in the cell chemotaxis detection and **-ized cellular segregation equipment in connection with this invention, and / the cell of specification / other wells ] -- putting in -- being concerned -- others -- it is concerned with the separation approach of the cell by extracting the cell which moved to the well.

[0018]

[Embodiment of the Invention] Two or more wells combine the cell chemotaxis detection and **-ized cellular segregation equipment in connection with this invention across passage, it is mutually open for free passage, and two tubing of tubing for avoiding the pressure up or reduced pressure by impregnation or extraction of tubing for pouring in or extracting a sample and a sample is formed in each well. Here, passage is a part which is making two wells open for free passage, and when a cell moves to the well of another side from one well, it is a path through which a cell passes. The equipment of this invention will be equipment which can detect the case where are hard to produce the liquid flow of the direction which goes to the well which faces in passage, and the liquid of the well in the both ends of passage is not mixed mutually, consequently a cell moves only according to an operation of a chemotactic factor chiefly in case a sample is poured in and extracted, and if drawing 1 (sectional view) and drawing 2 (bottom view) explain a principle, it will be as follows.

[0019] In drawing 1 and drawing 2 , it is the well to which 1 contains passage and 2 contains samples, such as cell suspension and a specimen solution, and a sample is supplied to a well 2 by the micropipette etc. through tubing 3, or is extracted from a well 2. the case where the specimen solution of a cell of the well (2B) of another side is a chemotactic factor when cell suspension is put into one of the wells 2 (2A) -- a well -- it is going to move toward 2B and passes through passage 1.

[0020] the cell suspension which is one of the samples -- a micropipette etc. -- tubing 3 -- leading -- a well -- the fluid pressure poured in in case 2A is supplied -- a cell -- passage 1 -- passing -- the well of the opposite side -- moving to 2B arises. When this aims at separation of a cell while migration of a cell becomes the factor which gives derangement to the judgment of being based on the chemotaxis which a specimen's has, other cells will be mixed into a desired cell and it will be given to the purpose. In order to solve this trouble, this invention forms tubing 4 so that it may be open for free passage with tubing 3, it misses the injection pressure which joins tubing 3 in the direction of tubing 4, and prevents that a cell flows compulsorily toward passage 1.

[0021] Similarly, in case a specimen solution is supplied to a well (2B) through tubing 3 by a micropipette etc., the situation which a specimen solution goes into the well (2A) of the opposite side through passage 1 with an injection pressure, and is mixed with cell suspension arises, and the phenomenon in which a cell passes through passage 1 by the chemotaxis is got confused thru/or checked. In order to prevent this, tubing 4 is formed also in the well (2B) which contains a specimen. By forming the tubing 4 which is open for free passage in this way in the tubing 3 which pours in a sample in this invention, effect of the fluid pressure to a horizontal direction can be made into min, and it can judge

more correctly whether a specimen solution has cell chemotaxis. The relaxation operation of differential pressure with tubing 4 is effective also when easing the reduced pressure at the time of extracting samples, such as a cell, from a well, and it makes extraction of a sample easy.

[0022] if drawing 1 explains the case where a sample is poured into a well in the equipment of this invention -- beforehand -- each -- a well and passage -- a cell isotonic solution -- filling -- a well -- the tubing 3 of 2A to cell suspension -- a well -- a chemotactic factor content solution is mostly poured in equivalent [ every ] from the tubing 3 of 2B, respectively. By carrying out like this, the pressure at the time of sample impregnation is eased with tubing 4.

[0023] Since it has tubing for avoiding the pressure up or reduced pressure by impregnation or extraction of a sample with tubing setting to the equipment of this invention, and for each well pouring in or extracting a sample, without it affects other wells -- each -- it is possible to pour a sample into a well, or to be able to extract a sample from a well, to make it join together in various formats [ for the purpose of this, therefore two or more wells ], and to make it mutually open for free passage. The format which two or more wells 2 join together through passage 1, and is mutually open for free passage can be variously adopted according to the purpose so that it may mention later ( drawing 12 - drawing 16).

[0024] the cell poured in when detecting the chemotaxis of a cell or dissociating -- the beginning and a well -- being collected near a bank or the passage inside is desirable. if the unit of the cell chemotaxis detection shown by drawing 1 or **-ized cellular segregation equipment is taken for an example -- tubing 3 -- letting it pass -- a well -- the cell poured into 2A -- a near bank, i.e., a well, -- existing near the passage which goes to 2B is desirable. the well which accommodation of this location faces through passage -- it can carry out by attracting a suitable quantity of a liquid at a suitable rate from the tubing 3 of 2B, or 4. The amount of the liquid to attract is calculated from the volume of tubing and a well. The amount and suction rate of the liquid to attract are easily controllable by the computer program.

[0025] It is desirable to establish the slot of the width of face doubled with the path of a cell as shown in drawing 4 thru/or 11, or its deformability in passage 1 for two or more [ 1 thru/or ], for example, the obstruction constituted about 100. It says passing through the slot of spacing with the deformability of a cell narrower than the path which it has in the configuration (spherical) which changes a form easily because of the resiliency, and takes gestalten, such as the shape of the shape of flat, or a string, and a cell usually takes in free space when a cell is what has resiliency here. By preparing this slot, it becomes possible to observe a cell on each level, and can dissociate for every class of request of a cell. In addition, drawing 3 shows the case where the obstruction 6 is established so that it may constitute the slot 5 which is illustrated by drawing 4 - drawing 11 in passage 1.

[0026] Counting of the number of cells under passage or after passage is performed in observation thru/or passage of migration of a cell by setting detection equipment, for example, a microscope, to passage 1, as shown in drawing 3 . Moreover, it becomes possible by combining a microscope-video camera or a CCD camera to record the progress which a cell moves automatically.

[0027] carrying out marking of the cell with luminescence and a fluorescent material beforehand according to the conventional method, and catching its luminescence and fluorescence, although the detection and counting of a cell which pass through passage 1 can also be performed by catching a cell under a direct microscope -- easy -- detection - counting can be carried out.

[0028] When the well equipped with the communicating tube mentioned above makes one unit the equipment which comes to be open for free passage through passage and makes two or more units accumulate, it can consider as the equipment which can detect to coincidence for the specimen of varieties, or the cell of varieties. Tubing for pouring in and extracting tubing and cell suspension for pouring in a specimen solution becomes possible [ carrying out the concurrency of the cell which does easy the activity by two or more micropipettes by making each unit accumulate so that it may stand in a line on a straight line or a concentric circle, respectively, and passes through each passage, and observing it ] (refer to drawing 17 - drawing 21, and drawing 25). Many samples can be processed at once in separation of a cell.

[0029] According to this invention, it becomes it is possible to miniaturize this whole equipment and possible to be able to process a sample in a minute amount, to make a majority of each units accumulate moreover, and to process an a large number specimen to coincidence. Furthermore, it is easy to carry out by automating by the program control of the suction and the injection rate of a liquid.

[0030] Automation of equipment namely, with a unit simple substance and the unit section which consists of the same, an accumulation unit to which it makes it come to accumulate two or more two or more sorts of units, or two or more accumulation units By having ****** which is equipped with sample supply pipets which move each part, such as the pipet washing section and this, a cell stores dept., a specimen stores dept., and if needed, such as a cell and a specimen, and controls actuation of pipets, such as this The whole equipment also including supply and extraction of a cell, a specimen, etc. can be controlled automatically. This control is easily performed by the computer program.

[0031] It will be as follows if the structure of the equipment in connection with this invention is explained still more concretely.
[0032] 1) passage 1 and a well 2 are built in one on a substrate 7 so that it may illustrate to structure drawing 1 and drawing 2 of a unit -- having -- a substrate 7 -- each -- hole (through tube) 3' connecting with two tubing which leads to a well, and 4' are prepared. The block 9 which dug the tubing 3 and 4 equivalent to through tube 3' of a substrate 7 and 4' fixes so that each tubing may agree in each through tube 3' on a substrate 7, and 4'. The glass substrate 8 which carried out optical polish is made to stick to the inferior surface of tongue of a substrate 7 by pressure. In addition, block 9, a substrate 7, and a glass substrate 8 may be stuck by pressure and fixed by binding tight with O ring etc. (refer to drawing 22).
[0033] 2) a well -- a well 2 contains specimen solutions, such as a sample, i.e., cell suspension, or a chemotactic factor content solution, and this inhibitor content solution, and especially a limit does not have the volume and it just contains necessary minimum volume. For example, it is enough if it is a depth of about 0.1mm, width of face of about 1.2mm, and die length of about 2.5mm.
[0034] intersecting perpendicularly with passage and establishing a wall in either of the wells which are mutually open for free passage through passage, for example, the well which contains a cell, and both sides, in order to restrict the amount of a liquid [ / near the passage ], or cell suspension -- a well -- it becomes easy it to become easy to adjust the physical relationship over the passage of an inner cell, or to adjust the flow of a specimen sample (drawing 23). Well 2A and 2B are open for free passage through passage 1, and drawing 23 shows the case where intersect perpendicularly with passage 1 and Walls 14A and 14B are formed in each well. the well from sample filling pipe 3A -- the time of a cell being poured into 2A -- a cell -- between wall 14A and passage 1 -- an assembly -- being easy . Although spacing of a wall 14 and passage 1 can be set as arbitration, it is usually chosen out of 50-300 micrometers.
[0035] The modification of the well which passage and drawing 24 crossed at right angles, and established the wall, and passage is shown. In the case where passage is established in a part of width of face of a well, as for (1), passage is bisected in the center, as for (2). while two wells (2B, 2C) are prepared to the well (2A) of a piece across passage -- a well -- as for (3), in passage, the train of an obstruction shows the 2 successive-installation eclipse ****** case for the case where the wall 24 is formed only in the 2A side, across the terrace 11, respectively. Such deformation is what was mentioned as instantiation, and it is not necessary to say not being restricted to this etc.
[0036] 3) It will be as follows if drawing 1 and drawing 3 explain an example of the structure of the passage passage 1. passage 1 -- the well of both ends -- 2A and a well -- it is constituted by the bank 10 (lobe on a substrate 7) and glass substrate 8 which separate 2B. As a desirable mode, two or more obstructions 6 which are illustrated by drawing 4 - drawing 11 are established on a bank, and the slot 5 through which a cell passes is formed.
[0037] A bank 10 does not separate the well 2 in the both ends of passage 1, and although about 1.2mm especially of the size is not limited, it should just have it about 0.01-1.0mm as die length in the direction which intersects perpendicularly in the direction which goes to the well which faces as die length in the direction which goes to the well which faces height of about 0.1mm, for example.
[0038] If an obstruction is inserted into the top face of a bank and a flat surface is established in it, it will become easy to observe passage of a cell (this flat surface will be called a terrace). Preparing is desirable although a terrace 11 ( drawing 3 ) is not indispensable. When forming a terrace 11, the lay length which goes to the well which faces is suitably chosen from about 0.03mm thru/or about 0.4mm.
[0039] in addition, the thing for which a terrace 11 is formed in a multistage type so that it may illustrate to drawing 26 -- one well -- the cell put into the well of another side when drawn in from the side -- the near bank 10 -- an assembly -- easy -- it becomes. When cells are neutrophil leucocyte, eosinophile leucocyte, basophilic leucocyte, etc., a terrace 11-2 and the distance (it sets to drawing and is the height of an obstruction 6) from the glass substrate 8 of 11-3 For example, 3 micrometers, the distance from a terrace 11-1 and the glass substrate 8 of 11-4 -- 4.5 micrometers -- carrying out -- a well -- 2A -- a cell -- putting in -- a well -- between the terrace 11-2 if liquid is attracted from 2B side, once, as for a cell, a terrace 11-1 will stop by the way, and glass substrates 8 -- an assembly -- easy -- it becomes. each -- although the distance from the glass substrate 8 of terrace 11-1-4 can be suitably set up according to the cell to deal with and it may be set up in the range which is 3 thru/or 5 micrometers in general, it is not necessarily limited to this. Here, about 1.5 thru/or observation of the cell which passed through the slot when lengthened 5 times, and counting can be more easily performed from the near terrace (terrace 11-2) of the well which contains a cell for the die length of the terrace (11-3) of the opposite side of the well which contains a cell. In addition, drawing 26 is a terrace 11-2, although the case where the obstruction 6 is established is shown. And when the distance from the glass substrate 6 of 11-3 is equivalent to the path or deformability of a cell, an obstruction is not necessarily required.
[0040] Although the cross section of the slot 5 constituted with an obstruction 6 can make the configuration of

arbitration a V character mold cross section, a concave cross section, a semicircle mold cross section, etc. when forming an obstruction 6 (drawing 3 - 5 reference) in the top face of a bank, a V character mold cross section is usually desirable. The width of face of a slot 5 is usually chosen from 3-50 micrometers, it is desirable that it is only the width of face which one target cell passes at a time, and suitable width of face is chosen according to the class of cell. In the case of an erythrocyte, neutrophil leucocyte, eosinophile leucocyte, basophilic leucocyte, monocyte and a macrophage, a T cell, a B cell, etc., it is chosen out of 3-10 micrometers, 6, 7, and 8, or 10 micrometers, and, in the case of the cell which exists in a cancer cell or an organization, width of face of 10-20 micrometers is chosen. [ for example, ] The number of slots 5 is about 10 thru/or about 50 more preferably about 5 thru/or 80 abbreviation 1 thru/or 100 abbreviation.

[0041] The die length of an obstruction 6 is chosen from about 10 - 400 micrometers of abbreviation, for example, 10, 20, 30, 40, 60,100,200,300, or a 400-micrometer thing is used. The width of face of obstruction 6 the very thing can be chosen suitably, and its about 2 times of the width of face of a slot 5 are usually desirable. When taking the structure shown in drawing 10, the one where die length in every direction is almost more nearly equal is effective.

[0042] The slot 5 which forms passage 1 may be mutually open for free passage in 1 thru/or two or more slots 12 which intersects perpendicularly in the direction which goes to the well which faces so that it may illustrate to drawing 6 - drawing 10. Signs that a cell passes can be more correctly grasped by [ which write ] carrying out. In that case, you may make it change gradually [ whenever it crosses drawing 8 and the slot 12 which intersects perpendicularly the width of face of a slot 5 with this like drawing 9 towards going to the well which faces ]. In addition, although drawing 8 shows the example from which the width of face of obstruction 6 the very thing changes, as shown in drawing 9 , the width of face of a slot 5 can also be changed by making the number of the obstructions 6 which have the same magnitude fluctuate.

[0043] Whenever two or more slots 5 of the direction which goes to the well which faces cross the slot 12 which intersects perpendicularly with this so that it may illustrate to drawing 10, mutual physical relationship is shifted, and it may be formed. Drawing 10 shows the case where change 1/2 pitch of physical relationship at a time, and it is formed, like 5a and 5b, whenever the slot 5 of the direction which goes to the well which faces crosses the slot 12 which intersects perpendicularly with it. The specimen solution which contains a chemotactic factor and inhibitor by making a slot 5 form in this way can be diffused, and while being able to distribute the specimen solution in the direction which goes to the passage which faces over homogeneity, it becomes possible to avoid more efficiently the pressure up and reduced pressure by impregnation and extraction of a cell or a specimen.

[0044] Furthermore, an obstruction 6 may be the continuation form connected in the direction which goes to the well which faces so that it may illustrate to drawing 11. Moreover, a terrace can be prepared in the center of a bank, the train of an obstruction can also be formed in two places across a terrace (refer to drawing 24 (3) and drawing 35), and observation and counting of the cell after passing through a slot are easily performed by considering as this structure. In addition, as for the magnitude of a central terrace, it is desirable that it is the magnitude which can be covered with the visual field of a microscope. In drawing 35, (1) is a plan and (2) is a sectional view.

[0045] Although its about 4.5 micrometers are desirable when the height (depth of flute) of an obstruction 6 is convenient in it being the depth settled in the depth of focus of the microscope at the time of observing migration of a cell, for example, is doubled with the depth of focus of a 10 to 40 times as many microscope as this, it does not need to be limited to this.

[0046] 4) It can be made to be able to join together further if needed, and the free passage format of the well through the free passage format passage of the well through passage can also be made to open for free passage, although drawing 1 , 2 ream type illustrated to drawing 2 , 3 ream type illustrated to drawing 12 can be considered. The so-called concentric format of having made two or more wells opening for free passage through passage around one well can also be taken so that it may illustrate to drawing 13 other than a tandem type like drawing 12 as a format of a free passage. As deformation of the type of drawing 13, it can also be made concentric circular like drawing 14. Drawing 14 is the example which made 3 ream type concentric circular, and drawing 15 is a sectional view.

[0047] In the case of drawing 13, tubing 3 is formed in through tube 3' of a substrate, and tubing 4 is formed in through tube 4'. a well -- 2A -- tubing 3 -- letting it pass -- cell suspension -- putting in -- a well -- two or more chemotactic factors can be searched to coincidence by putting various specimens into 2Bs 1-4. furthermore, the sample containing two or more sorts of cells -- a well -- it can perform separating a cell according to a class at once by putting into 2A (sorting). for example, a well -- the chemotactic factor corresponding to the class of cell is put into 2Bs 1-4, and the sample which contains [ two A] the cell of two or more sorts of central wells, for example, whole blood, is paid. a cell has each chemotactic factor -- each -- a well -- it moves toward 2Bs 1-4. after fixed time amount progress -- each -- a well -- a cell is extracted through the tubing 3 linked to through tube 3' from 2Bs 1-4. under the present circumstances,

a well -- the reduced pressure generated at the time of suction according to an operation of the tubing 4 linked to through tube 4' of 2Bs 1-4 -- a well -- the cell suspension of 2A -- a well -- flowing into 2Bs 1-4 is prevented temporarily.

[0048] the case of 3 ream type illustrated by drawing 12 -- a well -- 2A -- cell suspension and a well -- 2B -- inhibitor content liquid and a well -- three persons' relation can be investigated at once per two or more specimens by putting in 2C chemotactic factor content liquid.

[0049] The type which at least two wells (2B1 and 2B2) are opening for free passage with other common wells (2C) further through passage mutually among two or more wells which are open for free passage through passage to one well (2A) is illustrated by drawing 16. in this case, a well -- 2A -- cell suspension -- a well -- the specimen solution which contains a chemotactic factor in 2C -- putting in -- a well -- it can investigate by putting in the specimen solution which contains an inhibitor different, respectively in 2B1 and 2B2, comparing the property of each inhibitor under the same conditions.

[0050] 5) As the quality of the material of the production substrate 7 of a well and passage, micro processing is easy and a comparatively inactive silicon single crystal is desirable to a cell. The obstruction 6 and slot 5 of passage 1 are machined by etching, a photolithography, etc. which are used for this silicon single crystal by manufacture of an integrated circuit. Since a well 2 and through tube 3', and 4' are comparatively large if they are compared with an obstruction 6 or a slot 5, they are producible with the application of various known machining techniques. It can be used if construction of the detailed structure in passage is possible for hard glass, a rigid plastic, a metal, etc. besides a silicon single crystal. In addition, passage 1 and a well 2 may be produced and combined with according to, respectively.

[0051] When drawing 27 explains an example of a manufacture process, a slot 5 is made to form first, as shown in some silicon single crystal substrates (1) (2) and (3). Here, (2) is a plan and (3) is a sectional view in the broken-line section. Subsequently, it leaves a slot 5 and an obstruction 6, and only the barrier height (for example, 4.5 micrometers) investigates the whole (4). Then, leave a bank 10 in the center, investigate further, a well 2 is made to form, and through tube 3' and 4' are prepared in (5) and the last by the sand PURASUTO method etc. at the pars basilaris ossis occipitalis of a well (6). (7) is the plan of (6).

[0052] 6) A block and the tubing block 9 are parts which have tubing which leads to a well, as illustrated to drawing 1. If physically possible, through tube 3' of a well and 4' may be directly equipped with tubing, and a block is not required in that case. The cross section of tubing 3 and 4 is usually chosen from a square or a round shape. Although especially the size of tubing is not limited, in the case of a square, one side is good at about 1mm, and when circular, a diameter is good at about 1mm. 2mm - about 10mm [ from / when die length holds the capacity of cell suspension and a specimen solution ] is required.

[0053] The quality of the material which constitutes a block or tubing can be chosen from plastics or metals, such as glass and an acrylic, and tubing is easily produced by **** and others by the usual machining means, for example, a laser beam.

[0054] when pouring a cell or a specimen into each unit manually (manual), in order to do an activity easy -- the surroundings of the upper limit section of each filling pipe -- the path of a filling pipe -- large -- a funnel -- insertion of a pipet will become easy if it digs and hollows to the ** (drawing 28 (1) and 29 reference in (2)).

[0055] 7) The glass substrate glass substrate 8 enables observation of the cell which constitutes the space which is stuck to a substrate 7 by pressure and contains a liquid, and passes through passage, and holds transparence and smoothness optically so that it may illustrate to drawing 1. Moreover, it is desirable for a cell to paste up. If this purpose is suited, plastics, such as a transparence acrylic, can also be used besides glass. Although not limited, if there is 1-2mm especially of thickness, it is enough.

[0056] 8) It can consider as the equipment which arranges thru/or accumulates two or more units on one substrate, and processes an a large number specimen to coincidence by making into one unit two or more wells which were open for free passage through the array passage of many units. When arranging a unit same type to juxtaposition (for example, drawing 17 -18), being accumulated circularly (for example, drawing 20 -21) and arranging a unit of a different kind (for example, drawing 19), it is possible to carry out various arrangement thru/or accumulation if needed. Although the format of arrangement thru/or accumulation is explained based on each drawing below, from the first, this etc. is instantiation, is not limited to this etc. and can take various combination according to the purpose.

[0057] Drawing 17 and drawing 18 show the case where it is prepared on [ 12 ] one substrate 7 which is the square which is shown in drawing 1 and drawing 2 , and whose one side the unit two wells come to be open for free passage of a unit through passage is 16mm. A long side is arranged by 5.7mm and, as for the magnitude of one unit, the shorter side is arranged by 0.8mm, as for spacing of 1.2mm and a unit. In addition, by drawing 17, drawing 18 shows the case

where a through tube is circular, to through tube 3' and 4' which were prepared in the substrate 7 being a square.
[0058] Drawing 19 shows the case where accumulation of the a large number unit shown in drawing 16 or drawing 17 is made to accumulate further. That is, each of a quadrilateral which is expressed with A1-4, B1-4, and C1-4 in drawing 19 is the accumulation shown by drawing 17 or drawing 18. Here, A lines, B lines, and C line can be accumulation of the unit of a mutually different type.
[0059] Drawing 20 shows the case where the unit which 2 ream type became independent of is accumulated circularly. Drawing 21 is the sectional view. If magnitude is illustrated, the radial width of face of the width of face of 1.5mm and passage is 0.5mm, and, as for well 2A and 2B, the slot 5 of 10-micrometer width of face is formed. In this case, the radius of the circle as the whole unit is 5.0mm. According to the purpose, it is not necessary to say that magnitude is changeable.
[0060] When making the unit of these large number accumulate, block 9 can be constituted as one thing which connects tubing to all units, respectively, and a glass substrate 8 can also make it one sheet on the whole.
[0061] Drawing 25 shows the case where 12-piece accumulation arrangement of the unit of the type shown in drawing 23 is carried out.
[0062] Much drawing 22 shows an example in the case of assembling the cell chemotaxis detection and **-ized cellular segregation equipment on which the unit was made to accumulate. One block 9 which covers a cover cap 17, the substrate 7 and packing 16 which made many units accumulate between the middle base materials 21, and it is set, one glass substrate 8 is set between the middle base material 21 and the bottom base material 22, and it binds tight with a screw. The physical relationship of block 9 and a substrate 7 is prescribed by the middle base material 21, and is fixed by guide pin **** 19 prepared in the base of the guide pin 20 and block 9 which were formed in the middle base material 21. In addition, you may make it directly stuck by pressure in 9 5 blocks of substrates.
[0063] In addition, in drawing 22, it is also possible to arrange two or more units which assembled the whole at fixed spacing using the substrate 7 which prepared one pair of wells and passage. In this case, it is exchangeable serially for every unit.
[0064] 8) It will be as follows if an example is given and explained about the case where the equipment of servo mechanism this invention is automated. In addition, this is instantiation, and in order to attain the purpose of automation, it is not necessary to say that various modes can be adopted.
[0065] The example of the servo mechanism of the cell chemotaxis detection in connection with this invention and **-ized cellular segregation equipment is shown in drawing 29. In drawing 29, in U, a cell stores dept. and S show a specimen stores dept., and, as for the unit section and C, W shows the pipet washing section. Straight-line X-X' shows the example of the line of flow of the specimen supply pipet [ two or more (drawing six pieces) ] arranged at the row, and straight-line Y-Y' shows the example of the line of flow of the cell supply pipet [ two or more (drawing six pieces) ] arranged at the row. The unit section U is set to the line-of-flow location of a pipet. The cell is contained by the cell stores dept. C and various kinds of specimens are contained at the specimen stores dept. S. if an example of a motion of each pipet is explained, although it comes out, it is not necessary to say the thing like a less or equal which is not restricted to this In addition, not only glass but a metal, plastics, etc. can be used for the quality of the material of a pipet, choosing them suitably.
[0066] drawing 29 -- setting -- a cell supply pipet -- the cell suspension of the cell stores dept. C to the specified quantity -- drawing in -- a line-of-flow Y-Y' top -- up to the unit section U -- moving -- the well of each unit -- cell suspension is supplied to 2A through cell filling pipe 3A. Then, a cell supply pipet moves in order to suspend return and actuation in the location of C or to supply cell suspension to a consecutive unit. In addition, it is desirable to stir the cell suspension in the cell storage container 25, just before using discharge inhalation actuation of a cell supply pipet and carrying out suction extraction of the cell, since a cell precipitates under gravity.
[0067] Next, a specimen supply pipet attracts the specimen of the specified quantity from the specimen stores dept. S, moves to U in a line-of-flow X-X' top, and supplies a specimen through specimen filling pipe 3B. Then, a specimen supply pipet moves to the pipet washing section of W in a line-of-flow X-X' top, carries out repetitive pumping of the penetrant remover of a cleaning tank, and washes a pipet. Then, a pipet goes up on the oil level of a cleaning tank, and it moves in order to suspend actuation or to supply a specimen on a consecutive unit.
[0068] in addition, a specimen supply pipet -- before specimen supply actuation -- the well of drawing 29 -- the liquid of 2B side to the specified quantity -- drawing in -- a well -- it is desirable to make the actuation which collects near the bank the cells into which it is put by 2A perform.
[0069] The unit section U to which cell suspension and a specimen were supplied in this way moves in the direction of arrow-head => of drawing 29, and stops in the location where passage 1 agrees in a detecting element, and the condition of a cell is detected and recorded. The train of the following unit section U moves even to the line-of-flow

location of a pipet, and a series of above-mentioned actuation is repeated by migration of the unit section U. In addition, the unit section U can also be moved together with the specimen stores dept. S, and the train of the following unit section U and the specimen stores dept. S will move even to the line-of-flow location of a pipet by migration of the unit section U and the specimen stores dept. S in that case.

[0070] The cell stores dept. C may be a container for holding temporarily the cell supplied to the unit section U, and as long as it has the function, what kind of configuration is sufficient as a container. An example of the form of the cell stores dept. C is shown, two or more cell storage containers 25 are arranged corresponding to the arrangement of each unit and two or more cell supply pipets in the unit section U, drawing 30 makes impregnation of the cell to each container easy, and the inlet 26 for using a cell without futility is formed in the form of a slant face. Furthermore, cell suspension does not have futility in each container, and it is desirable to form the induction 27 for making it easy to enter in a container. If cell suspension is poured in by adopting such structure in the part of the arbitration of the cell stores dept. C, since cell suspension will be supplied to all containers, the time and effort poured into each container can be saved. Moreover, when cell suspension is taken out from a container, in order to lessen the amount which remains, it is desirable to extract the pars basilaris ossis occipitalis of a container thinly. In drawing 30, (1) is 'sectional view [ in / a perspective view and (2) and / in (3) / broken-line A-A' of drawing (2) ], and (4) is a sectional view in broken-line B-B' of drawing (2). [ a plan ]

[0071] The specimen stores dept. S is equipped with the container for holding temporarily the specimen supplied to the unit section U, and as long as it has the function, what kind of configuration is sufficient as a container. When the specimen of varieties is supplied to the unit section, each specimen is poured into the container of a specimen stores dept. by the handicraft which used the micropipette etc. in many cases, but in order to make manual impregnation easy in that case, it is desirable to prepare the inlet which has bigger opening than a container so that it may illustrate to drawing 31. Moreover, when a specimen sample is taken out from a container, in order to lessen the amount which remains, it is desirable to extract the pars basilaris ossis occipitalis of a container thinly (refer to drawing 31). As for a perspective view and (2), in drawing 31, (1) is [ a sectional view and (3) ] plans. In addition, in case a specimen is poured in by manual actuation, the condition that the point 15 of a pipet is inserted even in the interior of a container from an inlet is shown in drawing (2). The case where two or more specimen storage containers are arranged along with line-of-flow X-X' of a specimen supply pipet is shown in drawing 32. Spacing of a container can be doubled with spacing of the unit in the unit section U, if it arranges so that an inlet may become the opposite side by turns, as shown in drawing. In addition, a specimen storage container may be a square shape, shows the example to drawing 33 and shows the case where two or more specimen storage containers are arranged along with line-of-flow X-X' of a specimen supply pipet to drawing 33 (2).

[0072] The pipet used in the equipment of this invention has the desirable thing of a type which has a multi-channel syringe which migration, and suction and discharge of a liquid are controlled by the computer program, and is illustrated to drawing 34. Although the needle (point) of a pipet is made from glass, a metal, plastics, etc., what was manufactured with the quality of the material which has flexibility is desirable. (1) is a plan and (2) is a horizontal side Fig.

[0073] 9) The detection means used in detection means this invention is a means to detect the cell which moves in passage, or the cell after moving, and includes the means for recording a detection result if needed. If it is the means known in order to detect and record a cell, all are usable, for example, it is the combination of a microscope, a microscope, and a video camera etc. The structure which attached the CCD camera is also employable as an objective lens. In detection of an accumulation unit, it is desirable to adopt the structure where an objective lens carries out the sequential scan of the passage of each unit.

[0074] Although a detection means is usually set as the passage of a unit as shown in drawing 3, in the automatic gear on which the a large number unit was made to accumulate, the train of each unit can carry out sequential migration at the detecting element installed in the position, and it can also take the structure of performing detection and record. Detection is performed when a detector scans the passage of each unit located in a line on the straight line. The number of the detectors to scan one and plurality is sufficient as them. By [ which write ] carrying out, it becomes possible to correspond to many accumulation units with a comparatively small number of detection equipments.

[0075] carrying out marking of the cell with luminescence and a fluorescent material beforehand, and catching its luminescence and fluorescence according to a conventional method, although detection and counting of the cell after passage can also be performed by catching a cell under a direct microscope while passing through passage or -- easy -- detection - counting can be carried out.

[0076]

[Effect of the Invention] Since it is hard to produce change (pressure up) of a pressure horizontal at the time of sample

impregnation by having formed two tubing 3 and 4 in each of a well 2 according to the equipment of this invention, migration of the specimen by external pressure or a cell cannot take place easily, movement by own strength of a cell can be caught correctly, and the quantum and the qualitative result in which the operation of a chemotactic factor or an inhibitor and the property of a cell were made to reflect faithfully can be obtained.

[0077] Since the equipment of this invention does not require delicate accommodation on the occasion of impregnation of a sample, it is suitable for dealing with the sample of a minute amount. That is, it is possible to set the amount of the cell to be used to 1/10 thru/or 1/1000 compared with the Boyden chamber used conventionally. For example, when whole blood is used as a sample, when detecting the chemotaxis of neutrophil leucocyte, it is good in the blood of 0.1microl, and measurable in 1micro about l blood in eosinophile leucocyte, monocyte, or basophilic leucocyte.

[0078] Furthermore, on the occasion of impregnation of a liquid, there is a merit that detection equipment is easily automatable, from the place which does not require delicate adjustment.

[0079] Since it is hard to produce change (reduced pressure) of a horizontal pressure from the cell suspension containing two or more sorts of cells in extracting this through tubing from a well after moving only a specific cell, the delicate accommodation at the time of sampling is unnecessary, and technical skill is not required. Consequently, the target cell is exactly extractable.

[0080] When air bubbles are contained in infusion, in order that tubing for avoiding the pressure up or reduced pressure prepared in each well may play the role which misses air bubbles, it is rare to carry out counting of the air bubbles, and there are few errors in measurement and observation.

[0081] In the equipment of this invention, it becomes possible to catch each motion of a cell by forming the slot 5 of the width of face doubled with passage 1 at the path of a cell, or its deformability. Consequently, a cell is separable from the sample which can investigate chemotaxis and contains two or more sorts of cells about a part of various corpuscles contained in it using the sample containing two or more sorts of cells, for example, whole blood, without separating this beforehand for every class.

[0082] Since the unit unit of the equipment in connection with this invention can be made minute, it is easy for it to make many units accumulate, and it can assemble the equipment which can process an a large number specimen simultaneously. Moreover, it is easy to consider as the equipment with which impregnation and detection of a liquid were automated in that case.

[0083] In making many units accumulate, by making it accumulated combining the unit of a different type, detection and separation which differs in the purpose can be performed to coincidence, and it becomes possible to gather the effectiveness of processing. For example, when investigating the chemotaxis of a cell which is different about the same chemotactic factor when performing various chemotactic factors or retrieval of the inhibitor to the cell of the same kind, it becomes possible to perform the retrieval at once.

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[Translation done.]

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DRAWINGS

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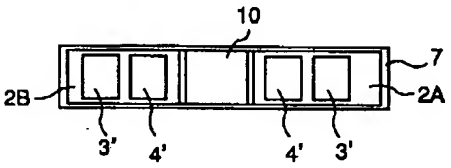
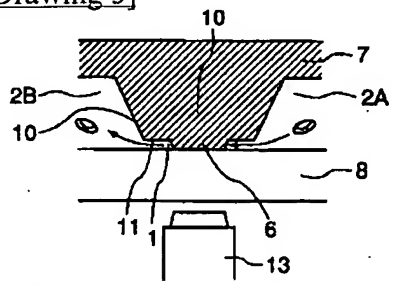
[Drawing 2]

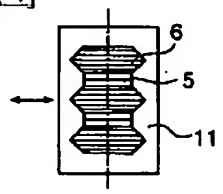



[Drawing 3]



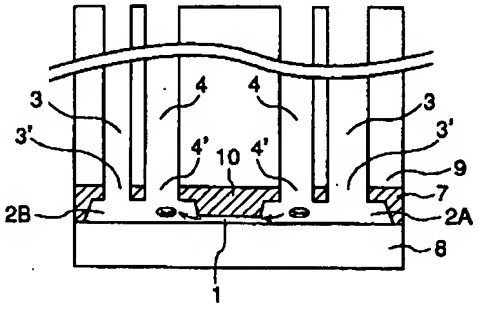

6: 隙盤
11: ﾃﾗｽ
13: 検出器

[Drawing 4]



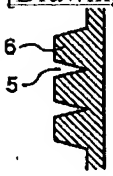

5: 流路を挟んで相対するｳｪﾙに向かう方向の流

[Drawing 1]

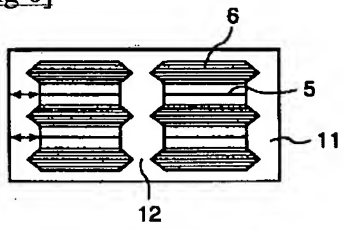



1: 流路
2: ウェル
3: 試料注入・採取用管
3': 管3に対応する貫通孔
4: 試料の注入・採取時における昇圧・減圧を回避するための管
4': 管4に対応する貫通孔
7: 基板
8: ガラス基板
9: 管を穿ったブロック
10: 土手

[Drawing 5]

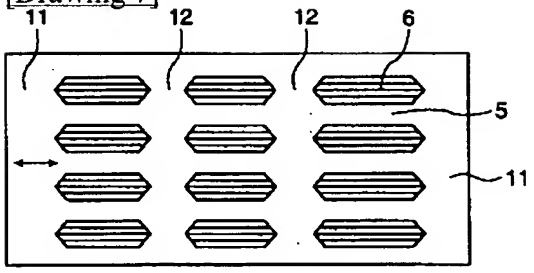



[Drawing 6]

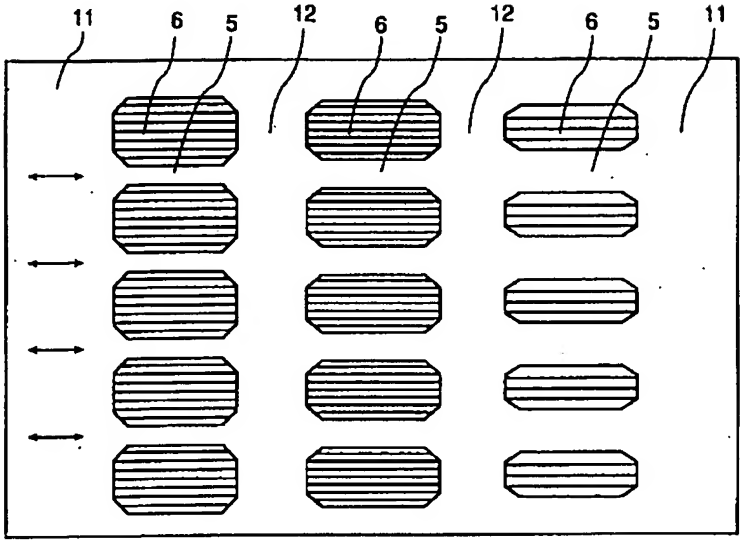



12: 溝5に直交する溝

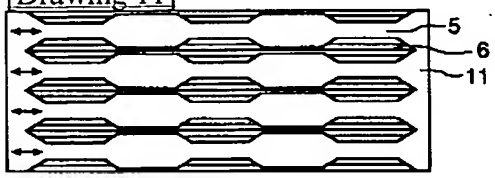
[Drawing 7]



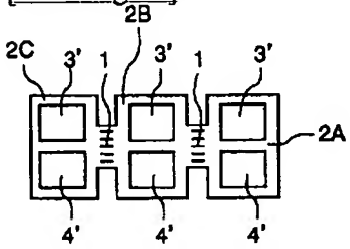

[Drawing 8]



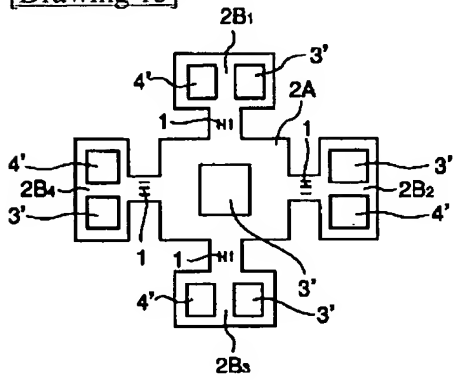

[Drawing 11]




[Drawing 12]




[Drawing 13]

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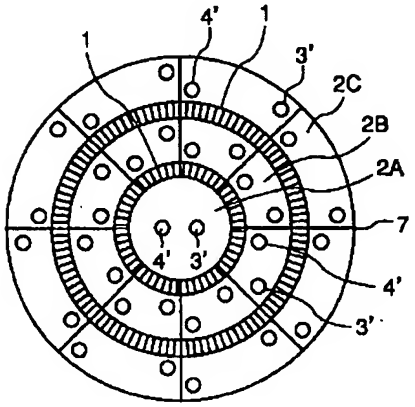
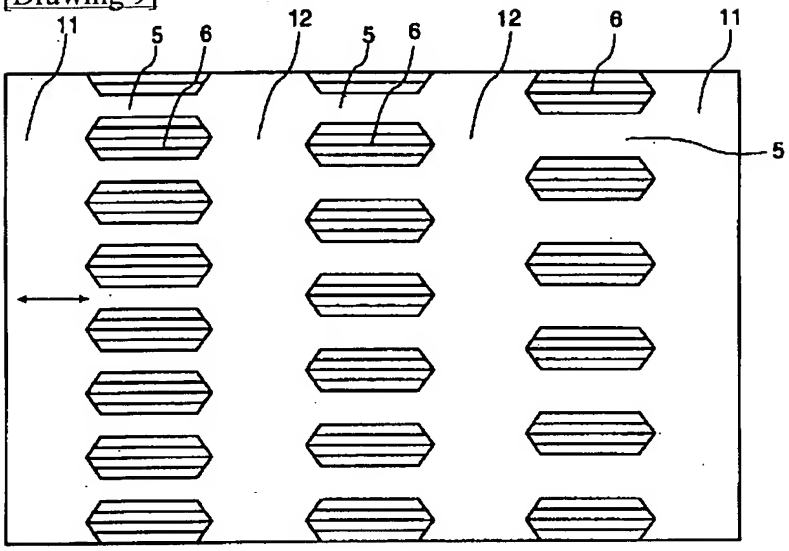
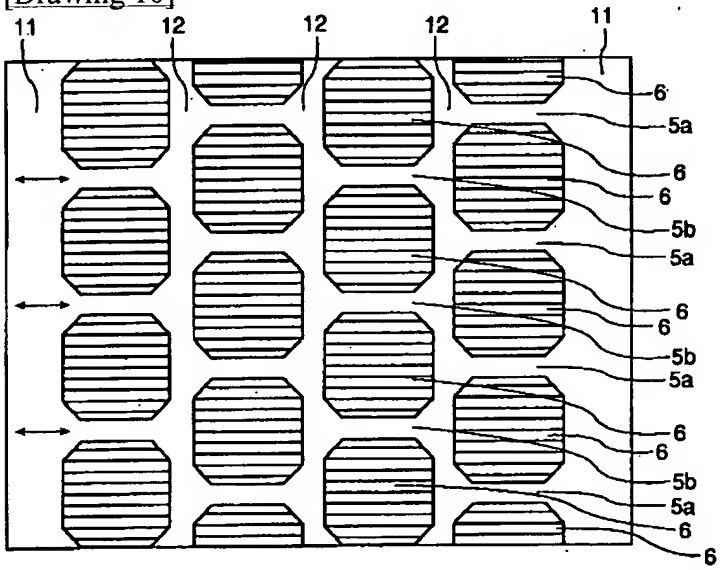



[Drawing 9]




[Drawing 10]

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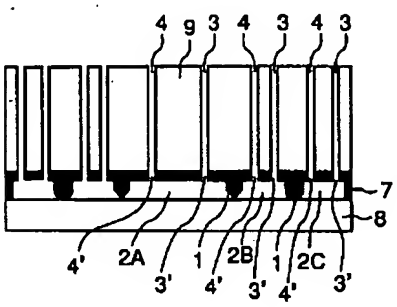
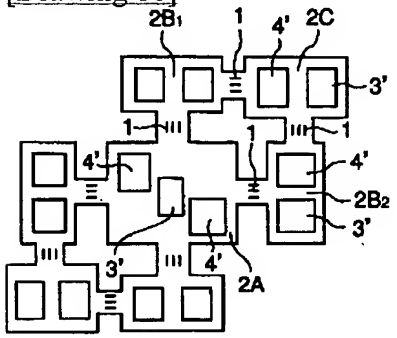
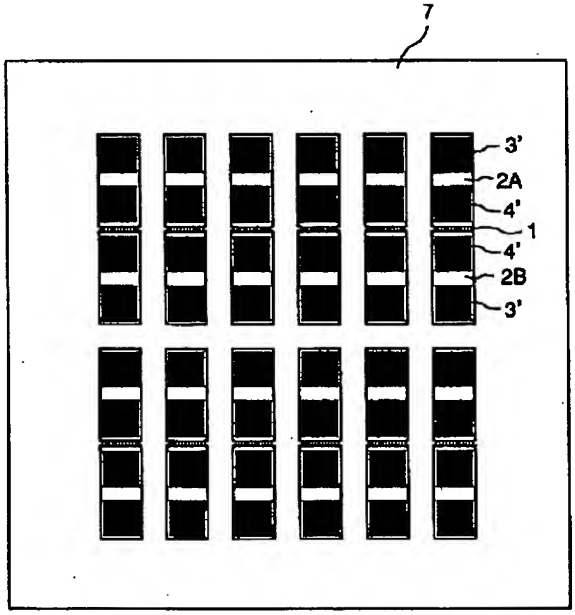


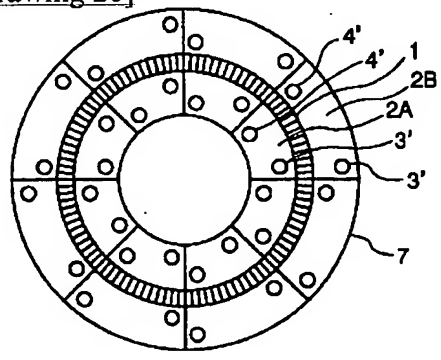

[Drawing 16]



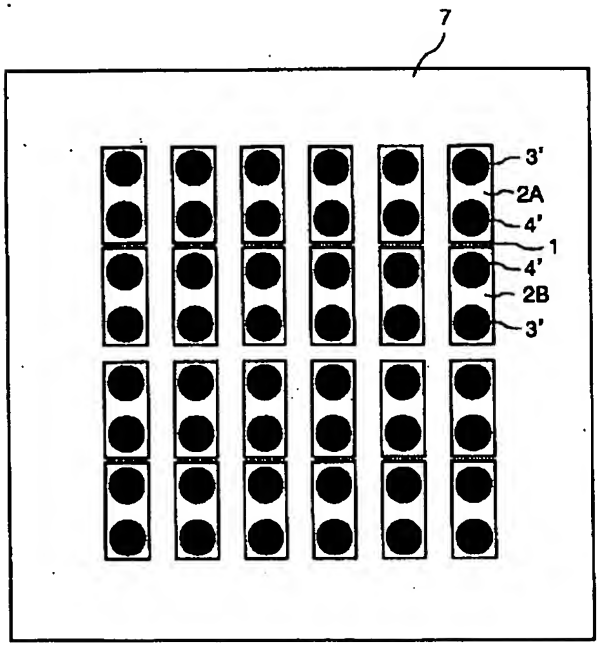

[Drawing 17]



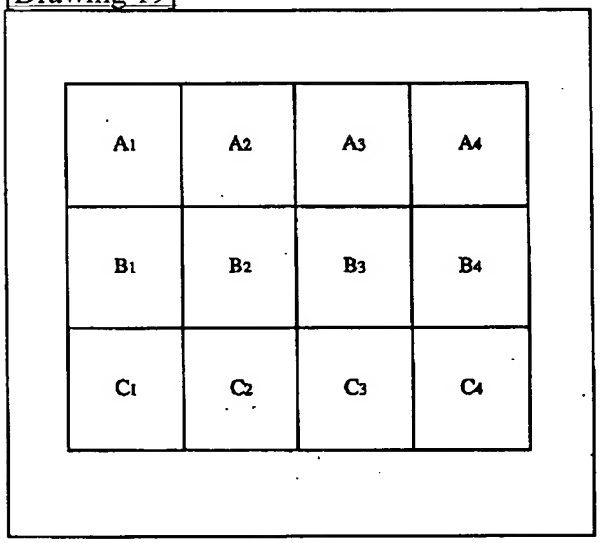

[Drawing 20]



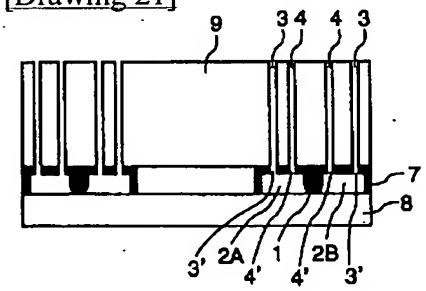

[Drawing 18]



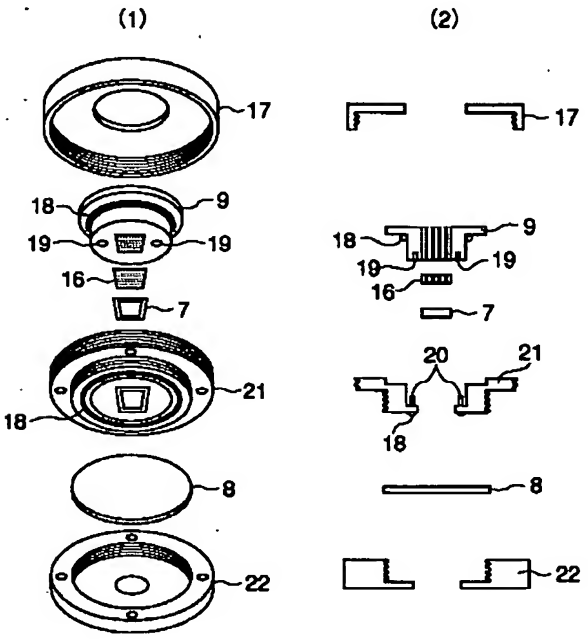

[Drawing 19]



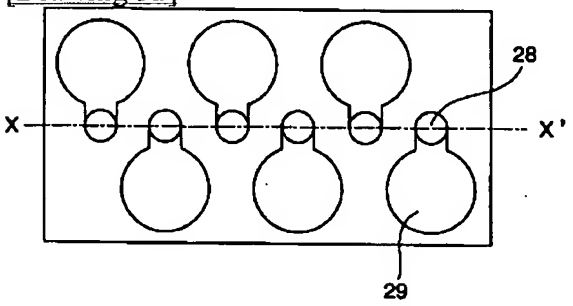

[Drawing 21]



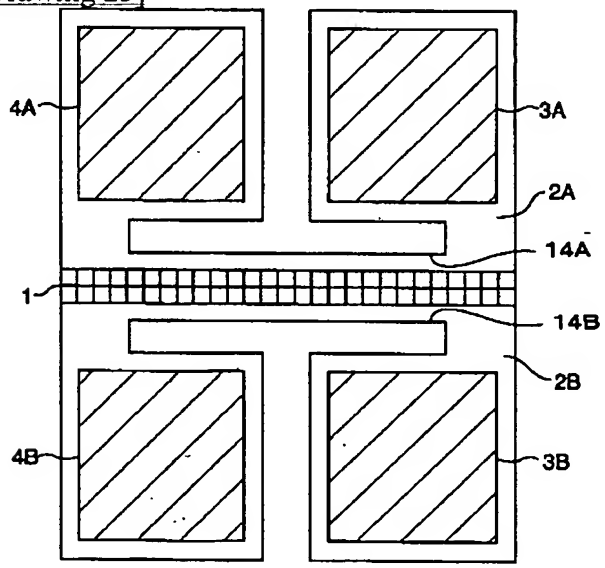

[Drawing 22]




[Drawing 32]

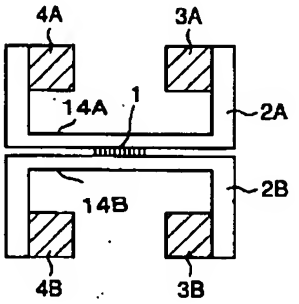



[Drawing 23]

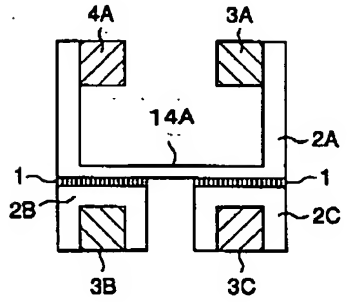



[Drawing 24]

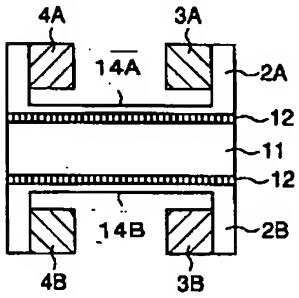
(1)



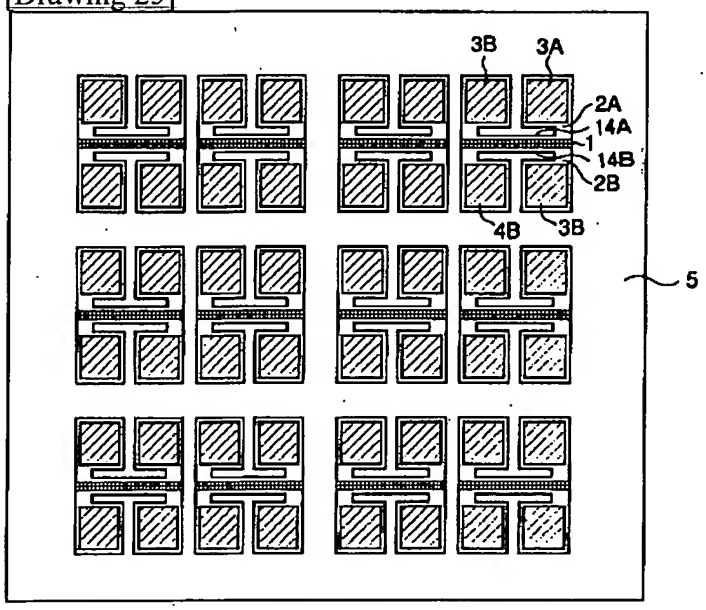

(2)



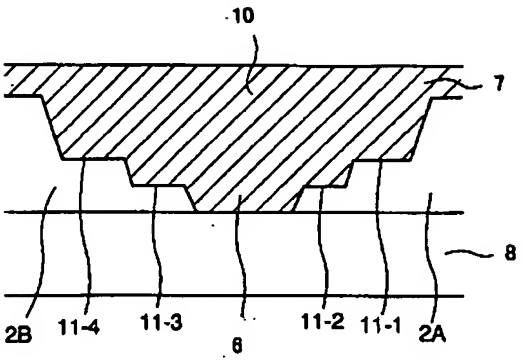

(3)



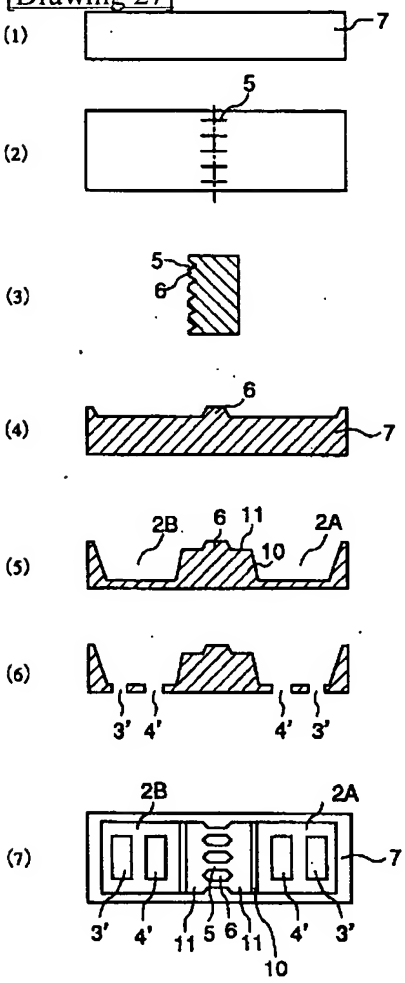

[Drawing 25]




[Drawing 26]

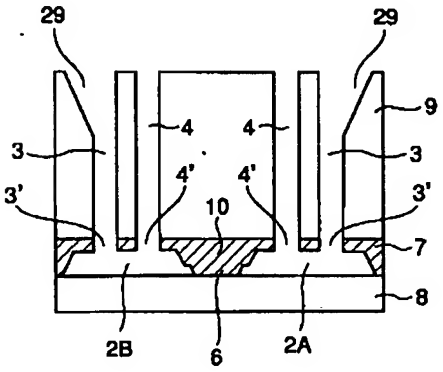



[Drawing 27]

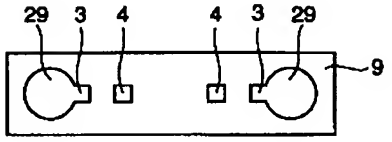



[Drawing 28]

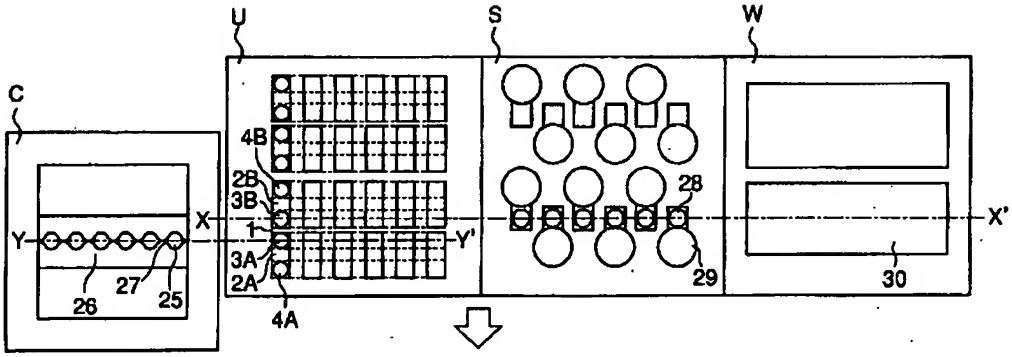
(1)



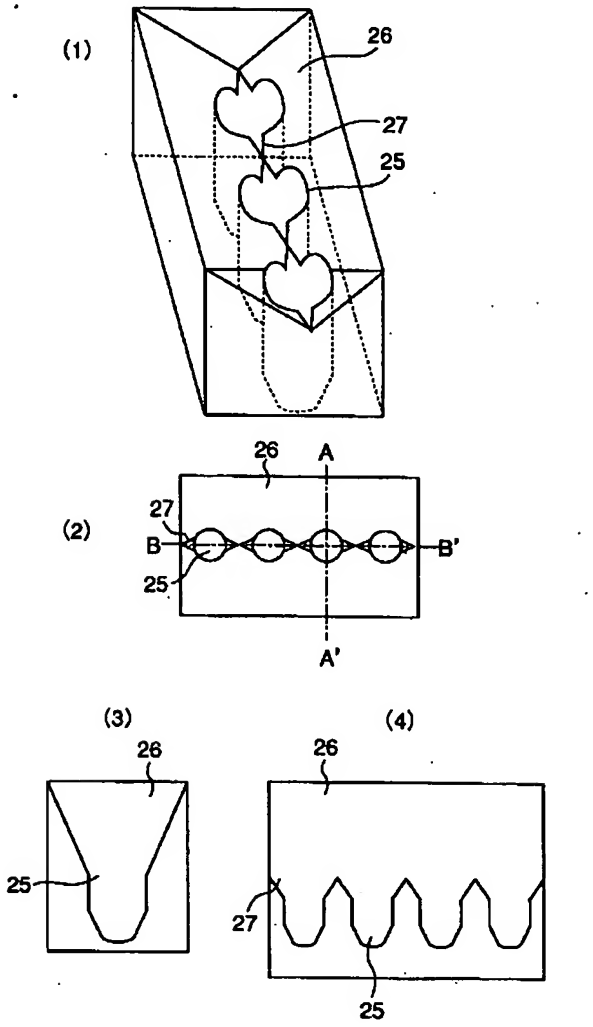

(2)



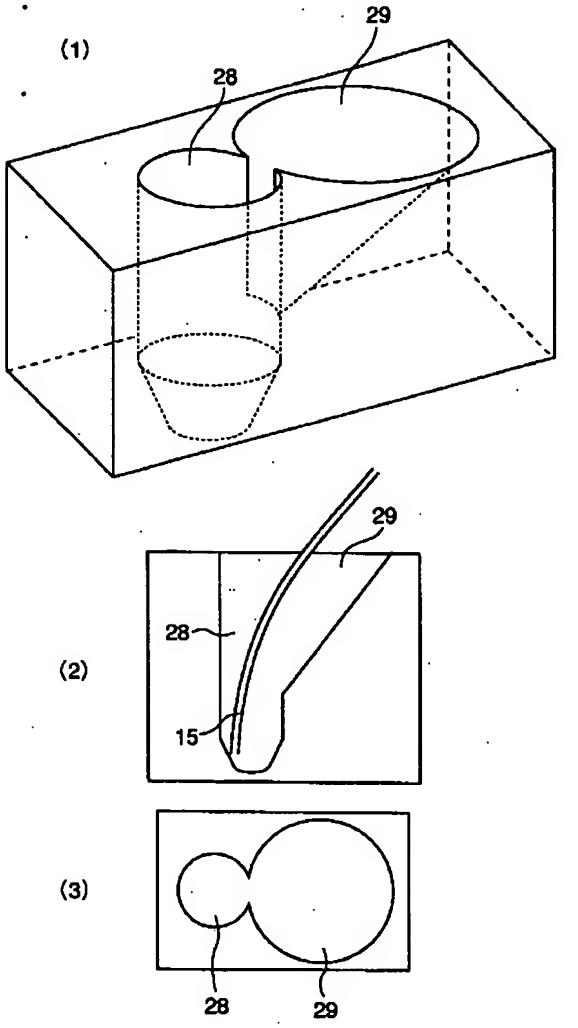

[Drawing 29]



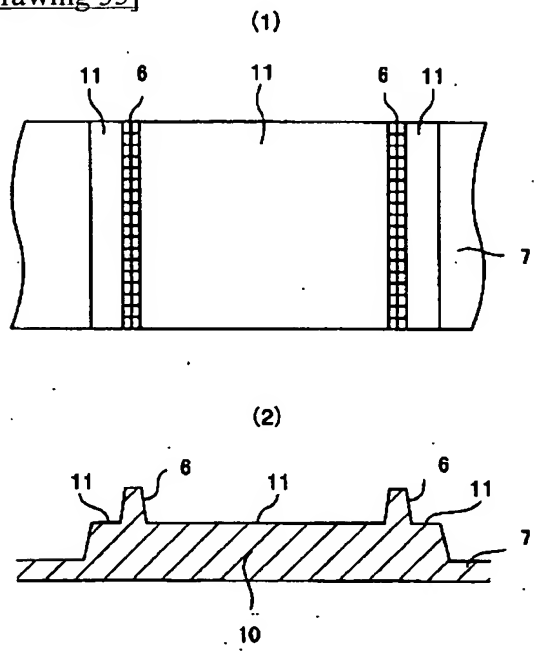

[Drawing 30]




[Drawing 31]

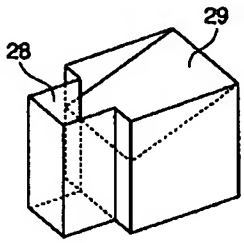



[Drawing 35]

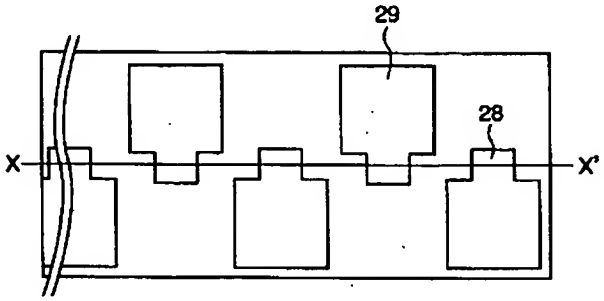



[Drawing 33]

(1)

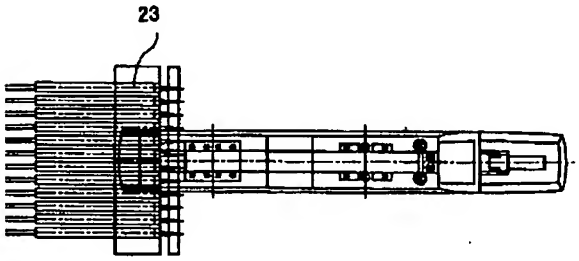



(2)




[Drawing 34]

(1)

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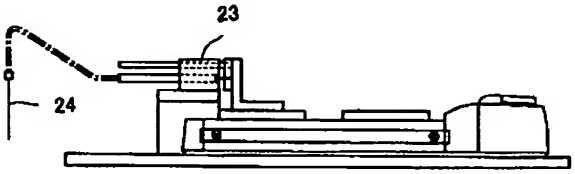


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[Translation done.]